

What is claimed is:

1. A product for repair of cartilage lesions, comprising:

a. a cartilage repair matrix suitable for conforming to a defect in cartilage; and

b. a cartilage-inducing composition associated with said matrix comprising a mixture of proteins comprising: transforming growth factor β 1 (TGF β 1), bone morphogenetic protein (BMP)-2, BMP-3, and BMP-7;

wherein the quantity of said TGF β 1 in said mixture is from about 0.01% to about 99.99% of total proteins in said mixture;

wherein the quantity of said BMP-2 in said mixture is from about 0.01% to about 10% of total proteins in said mixture;

wherein the quantity of said BMP-3 in said mixture is from about 0.1% to about 15% of total proteins in said mixture; and,

wherein the quantity of said BMP-7 in said mixture is from about 0.01% to about 10% of total proteins in said mixture.

2. A product for repair of cartilage lesions, comprising:

a. a cartilage repair matrix; and

b. a cartilage-inducing composition associated with said matrix comprising a mixture of proteins comprising:

(i) a bone-derived osteogenic or chondrogenic formulation containing at least one bone morphogenetic protein (BMP); and,

(ii) an exogenous TGF β protein;

wherein the ratio of said exogenous TGF β protein to said at least one BMP is greater than about 10:1; and,

wherein said exogenous TGF β protein is present in an amount sufficient to increase cartilage induction by said composition over a level of cartilage induction by said bone-derived osteogenic or chondrogenic protein formulation in the absence of said exogenous TGF β protein.

3. A product for repair of cartilage lesions, comprising:

- a. a cartilage repair matrix; and
- b. a cartilage-inducing composition associated with said matrix comprising a mixture of proteins comprising:

- (i) a TGF β protein; and,
- (ii) at least one bone morphogenetic protein (BMP);

wherein the ratio of said TGF β protein to said BMP protein is greater than about 10:1.

4. The product of any one of Claims 1, 2, or 3, wherein said mixture of proteins comprises TGF β superfamily proteins: TGF β 1, bone morphogenetic protein (BMP)-2, BMP-3, and BMP-7, wherein said TGF β superfamily proteins comprise from about 0.5% to about 99.99% of said mixture of proteins.

5. The product of Claim 4, wherein said TGF β superfamily proteins comprise from about 0.5% to about 25% of said mixture of proteins.

6. The product of Claim 4, wherein the quantity of said TGF β 1 in said mixture is from about 0.01% to about 75% of total proteins in said mixture.

7. The product of Claim 4, wherein the quantity of said TGF β 1 in said mixture is from about 33% to about 99.99% of total proteins in said mixture.

8. The product of Claim 4, wherein said mixture of proteins further comprises at least one bone matrix protein selected from the group consisting of osteocalcin, osteonectin, bone sialoprotein (BSP), lysyloxidase, cathepsin L pre, osteopontin, matrix GLA protein (MGP), biglycan, decorin, proteoglycan-chondroitin sulfate III (PG-CS III), bone acidic glycoprotein (BAG-75), thrombospondin (TSP) and fibronectin; wherein said bone matrix protein comprises from about 20% to about 98% of said mixture of proteins.

9. The product of Claim 4, wherein said mixture of proteins further comprises at least one growth factor protein selected from the group consisting of fibroblast growth factor-I (FGF-I), FGF-II, FGF-9, leukocyte inhibitory factor (LIF), insulin, insulin growth factor I (IGF-I), IGF-II, platelet-derived growth factor AA (PDGF-AA), PDGF-BB, PDGF-

AB, stromal derived factor-2 (SDF-2), pituitary thyroid hormone (PTH), growth hormone, hepatocyte growth factor (HGF), epithelial growth factor (EGF), transforming growth factor- α (TGF α) and hedgehog proteins; wherein said growth factor protein comprises from about 0.01% to about 50% of said mixture of proteins.

10. The product of Claim 4, wherein said composition further comprises one or more serum proteins.

11. The product of any one of Claims 1, 2 or 3, wherein said mixture of proteins comprises TGF β 1, TGF β 2, TGF β 3, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, CDMP, FGF-1, osteocalcin, osteonectin, BSP, lysyloxidase, cathepsin L pre, albumin, transferrin, Apo A1 LP and Factor XIIIb.

12. The product of any one of Claims 1, 2 or 3, wherein said mixture of proteins comprises Bone Protein (BP).

13. The product of any one of Claims 1, 2 or 3, wherein said cartilage-inducing composition is at a concentration of from about 0.5% to about 33% by weight of said product.

14. The product of Claim 1, wherein said mixture of proteins, when used at a concentration of at least about 10 μ g per 6.5-7.3 mg of bovine tendon collagen in a rat subcutaneous assay, induces a bone score of from about 1.0 to about 3.5, using a bone grading scale set forth in Table 8, and induces a cartilage score of at least about 1.2, using a cartilage grading scale set forth in Table 9.

15. The product of any one of Claims 2 or 3, wherein said composition, when used at a concentration of at least about 10 μ g per 6.5-7.3 mg of bovine tendon collagen in a rat subcutaneous assay, induces a bone score of less than about 2.0, using a bone grading scale set forth in Table 8, and induces a cartilage score of at least about 2.0, using a cartilage grading scale set forth in Table 9.

16. The product of Claim 2, wherein said exogenous TGF β protein is TGF β 1.

17. The product of any one of Claims 1 or 16, wherein the ratio of TGF β 1 to all other proteins in said mixture of proteins is at least about 1:10.

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18. The product of any one of Claims 1 or ⁵16, wherein the ratio of TGFβ1 to all other proteins in said mixture of proteins is at least about 10:1.

19. The product of any one of Claims 2 or 3, wherein the ratio of said TGFβ protein to said BMP protein is greater than about 100:1.

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20. The product of Claim ¹⁰3, wherein said TGFβ protein is TGFβ1.

^{Sub B2} → 21. The product of Claim 3, wherein said BMP protein is selected from the group consisting of BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, BMP-8, BMP-9 and CDMP.

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22. The product of any one of Claims 1, ⁴2 or ¹⁰3, wherein said cartilage repair matrix is bioresorbable.

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23. The product of Claims 1, ⁴2 or ¹⁰3, wherein said cartilage repair matrix comprises collagen from bovine tendon.

24. A method for repair of cartilage lesions, comprising implanting and fixing into a cartilage lesion a product comprising:

a. a cartilage repair matrix suitable for conforming to a defect in cartilage; and

b. a cartilage-inducing composition associated with said matrix comprising a mixture of proteins comprising: transforming growth factor β1 (TGFβ1), bone morphogenetic protein (BMP)-2, BMP-3, and BMP-7;

wherein the quantity of said TGFβ1 in said mixture is from about 0.01% to about 99.99% of total proteins in said mixture;

wherein the quantity of said BMP-2 in said mixture is from about 0.01% to about 10% of total proteins in said mixture;

wherein the quantity of said BMP-3 in said mixture is from about 0.1% to about 15% of total proteins in said mixture; and,

wherein the quantity of said BMP-7 in said mixture is from about 0.01% to about 10% of total proteins in said mixture.

25. A method for repair of cartilage lesions, comprising implanting and fixing into a cartilage lesion a product comprising:

- a. a cartilage repair matrix; and,
- b. a cartilage-inducing composition associated with said matrix comprising a mixture of proteins comprising:

- (i) a bone-derived osteogenic or chondrogenic formulation of proteins containing at least one bone morphogenetic protein (BMP); and,
- (ii) an exogenous TGF β protein;

wherein the ratio of said exogenous TGF β protein to said at least one BMP is greater than about 10:1; and,

wherein said exogenous TGF β protein is present in an amount sufficient to increase cartilage induction by said composition over a level of cartilage induction by said bone-derived osteogenic or chondrogenic protein formulation in the absence of said exogenous TGF β protein.

26. A method for repair of cartilage lesions, comprising implanting and fixing into a cartilage lesion a product comprising:

- a. a cartilage repair matrix; and,
- b. a cartilage-inducing composition associated with said matrix comprising a mixture of proteins comprising:
 - (i) a TGF β protein; and,
 - (ii) at least one bone morphogenetic protein (BMP);

wherein the ratio of said TGF β protein to said BMP protein is greater than about 10:1.

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27. The method of Claim 25, wherein said TGF β protein is TGF β 1.

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28. The method of any one of Claims 24 or 27, wherein the ratio of TGF β 1 to all other proteins in said mixture of proteins is at least about 1:10.

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29. The method of any one of Claims 24 or 27, wherein the ratio of TGF β 1 to all other proteins in said mixture of proteins is at least about 10:1.

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30. The method of Claim ³¹26, wherein said TGF β protein is TGF β 1.

31. The method of any one of Claims 25 or 26, wherein the ratio of said TGF β protein to said BMP protein is greater than about 100:1

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³² 32. The method of any one of Claims ²⁶24, ³⁴25 or ³¹26, wherein said cartilage lesion is an articular cartilage lesion.

33. The method of any one of Claims 24, 25 or 26, wherein said cartilage lesion is a meniscal cartilage lesion.

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³⁴ 34. The method of Claim ³⁴33, wherein said lesion is a vascular meniscus lesion.

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³⁵ 35. The method of Claim ³⁴33, wherein said lesion is an avascular meniscus lesion.

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³⁶ 36. The method of any one of Claims ²⁶24, ³¹25 or ³¹26, wherein said lesion is a tear and wherein said matrix is configured as a sheet, wherein said step of implanting comprises inserting said product directly into said tear.

37. A method for repair of segmental cartilage lesions, comprising implanting and fixing into a segmental cartilage lesion:

a. a first product comprising:

(i) a cartilage repair matrix configured as a sheet; and

(ii) a cartilage-inducing composition associated with said matrix comprising a mixture of proteins comprising: transforming growth factor β 1 (TGF β 1), bone morphogenetic protein (BMP)-2, BMP-3, and BMP-7;

wherein the quantity of said TGF β 1 in said mixture is from about 0.01% to about 99.99% of total proteins in said mixture;

wherein the quantity of said BMP-2 in said mixture is from about 0.01% to about 10% of total proteins in said mixture;

wherein the quantity of said BMP-3 in said mixture is from about 0.1% to about 15% of total proteins in said mixture; and,

wherein the quantity of said BMP-7 in said mixture is from about 0.01% to about 10% of total proteins in said mixture.; and,

b. a second product comprising a cartilage repair matrix configured to replace cartilage removed from said segmental defect;

wherein said first product is implanted between an edge of said lesion and said second product to provide an interface between said lesion and said second product.

38. The method of Claim 37, wherein said second product further comprises a cartilage-inducing composition associated with said matrix comprising a mixture of proteins comprising: transforming growth factor β 1 (TGF β 1), bone morphogenetic protein (BMP)-2, BMP-3, and BMP-7;

wherein the quantity of said TGF β 1 in said mixture is from about 0.01% to about 99.99% of total proteins in said mixture;

wherein the quantity of said BMP-2 in said mixture is from about 0.01% to about 10% of total proteins in said mixture;

wherein the quantity of said BMP-3 in said mixture is from about 0.1% to about 15% of total proteins in said mixture; and,

wherein the quantity of said BMP-7 in said mixture is from about 0.01% to about 10% of total proteins in said mixture.